Microarray data analysis – two approaches

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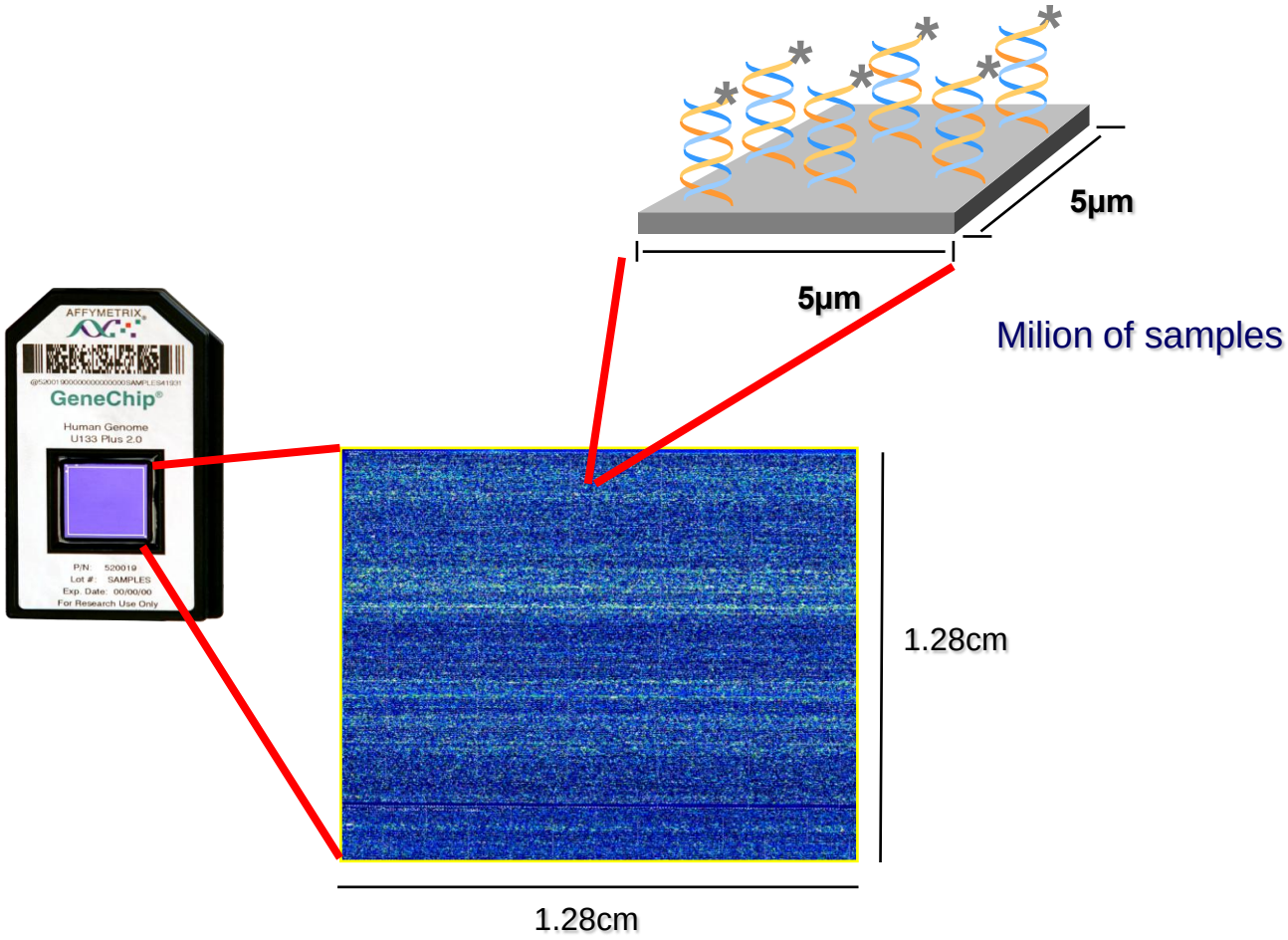
Outline

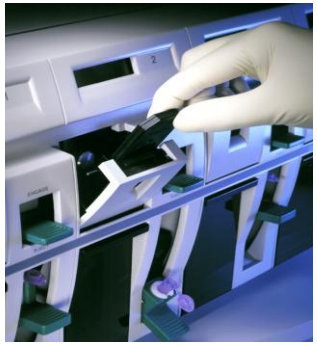
1. Microarray technique - introduction
2. Structure of experiment
3. Two methods of microarray analysis
   - Measurement of assotiation: genes-biological issue
   - Bayesian Networks procedure for creation of genes-biological issue depedence networks
4. Virolab – enviroment for microarray analysis

Microarray technique



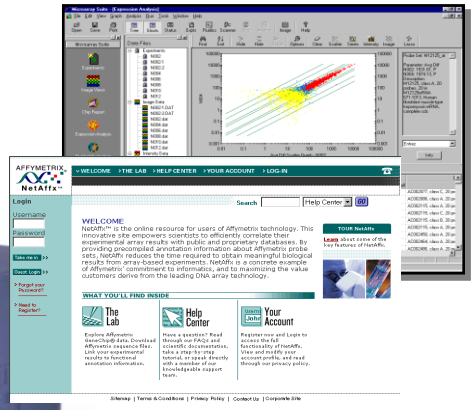
Microarray technique

Microarray (chips)



Fluidics Station

Scaner



Analysis

Micoarray technique - application

Microarrays can be used:

- **to measure changes in expression levels**
- **to detect single nucleotide polymorphism (SNPs)**
- **in genotyping**
- **in resequencing mutant genomes**

Microarray technique - application

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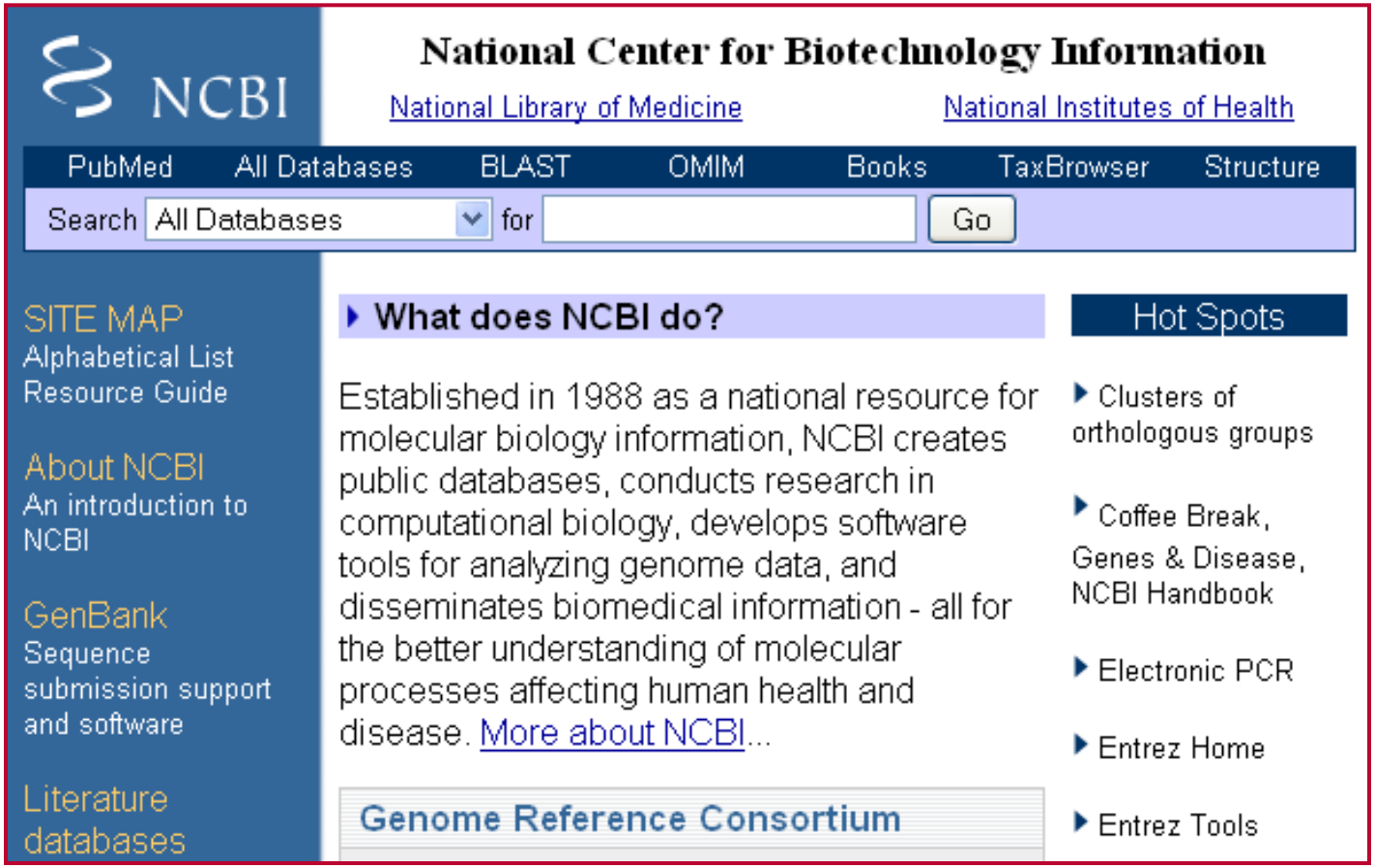
- **in resequencing mutant genomes**

It helps:

• to discover and understand disease pathways

• to develop better methods of detection, treatment, and prevention

NCBI/GEO – source of microarray data



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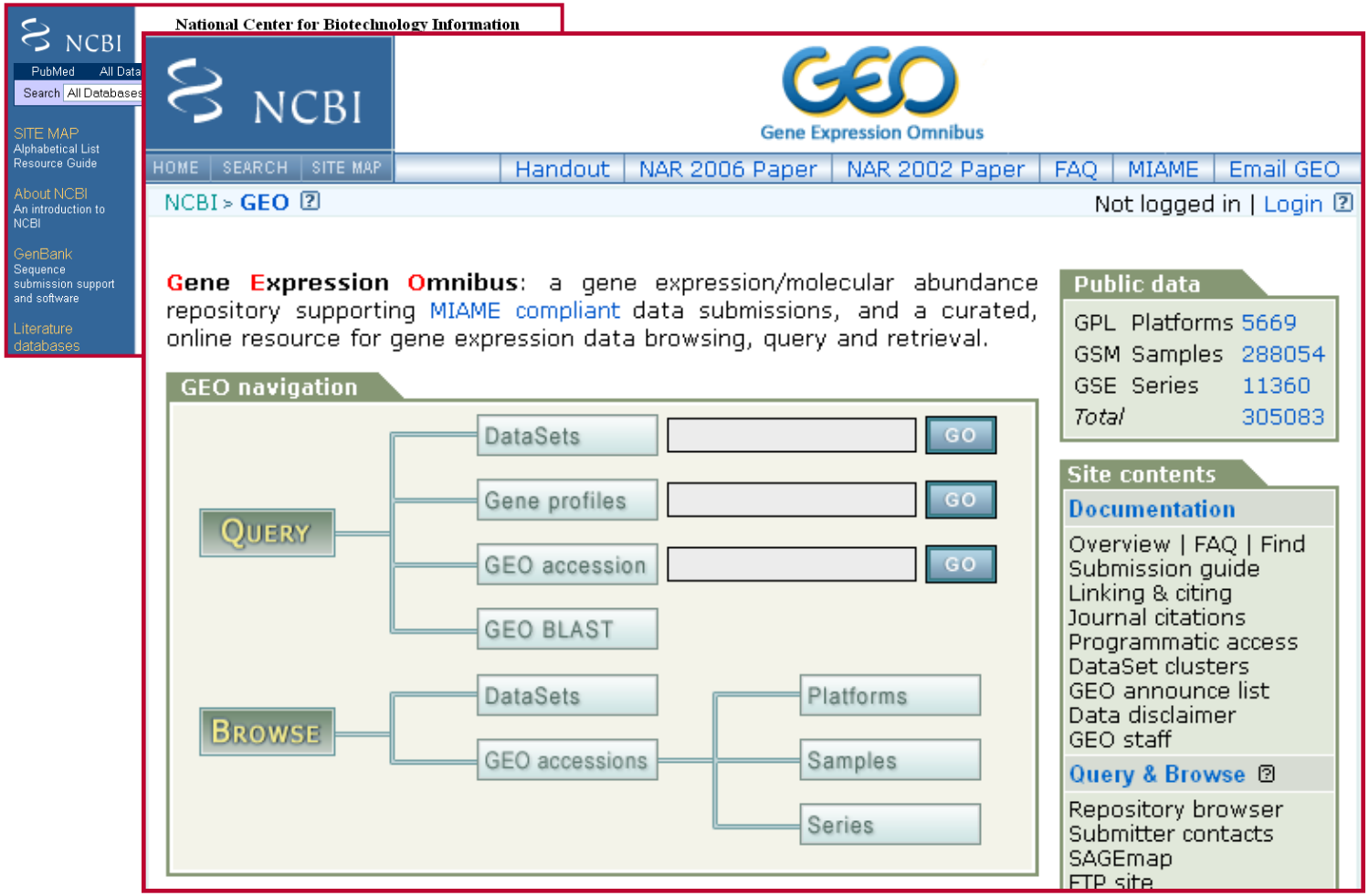

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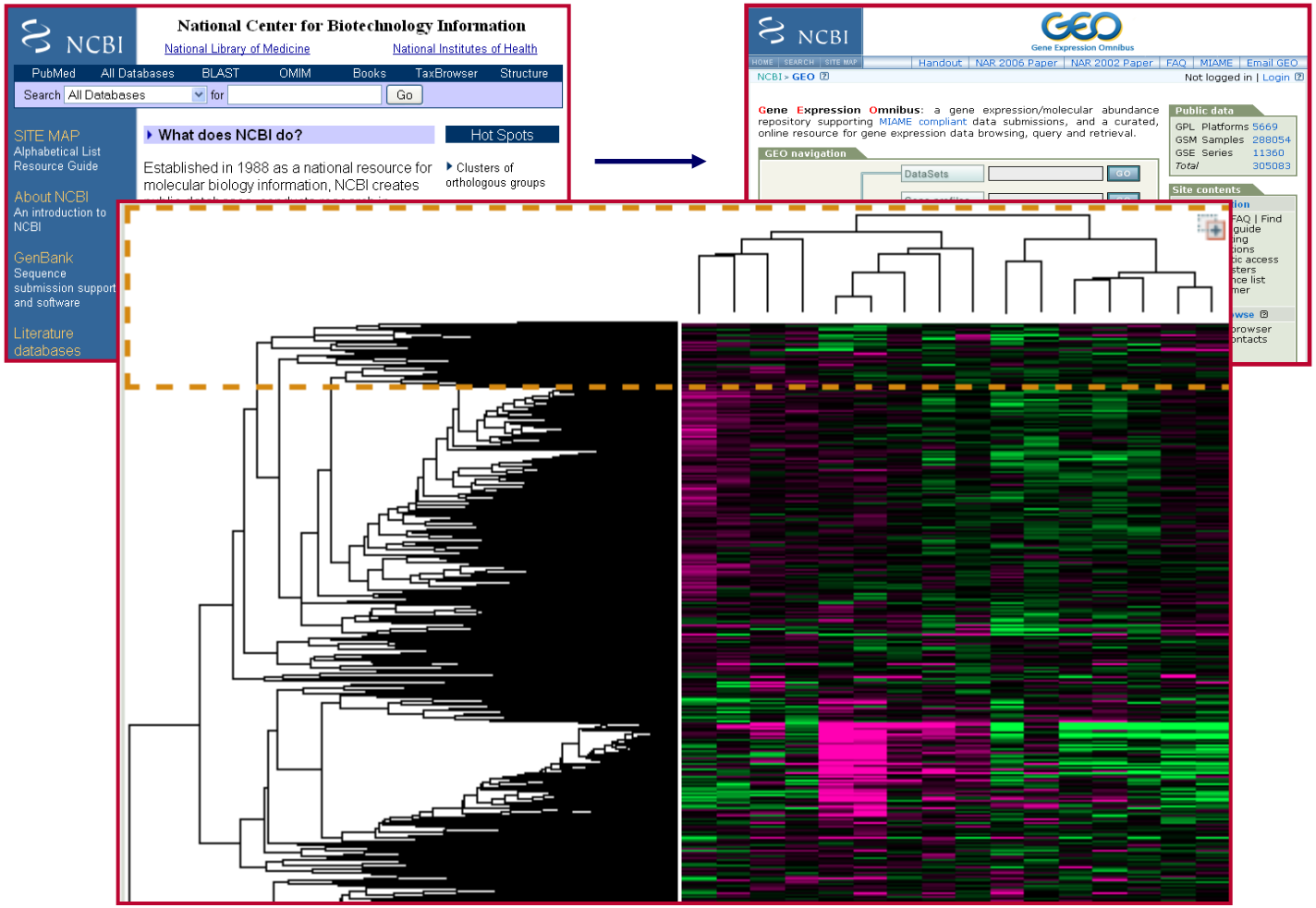

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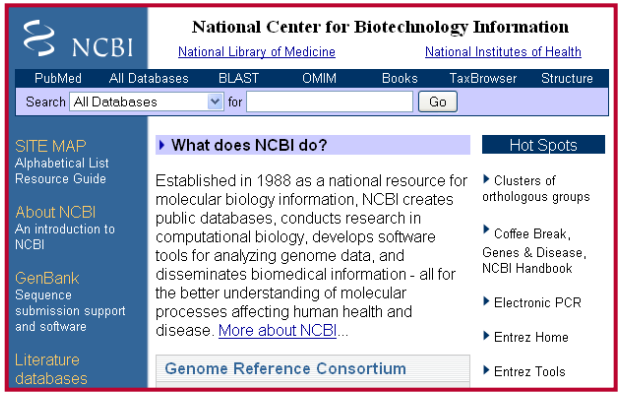
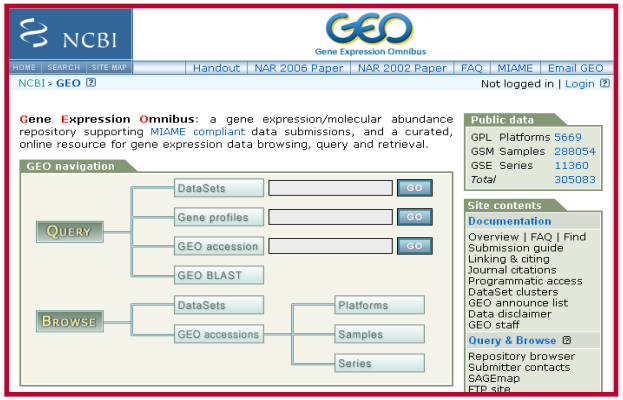
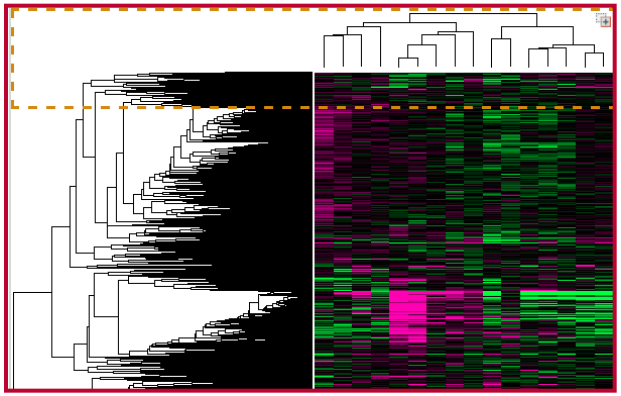






Gene Expression Omnibus:
a gene expression/molecular abundance repository

GPL	Platforms	5669
GSM	Samples	288095
GSE	Series	11372
Total		305136

http://www.ncbi.nlm.nih.gov/geo/info/MIAME.html

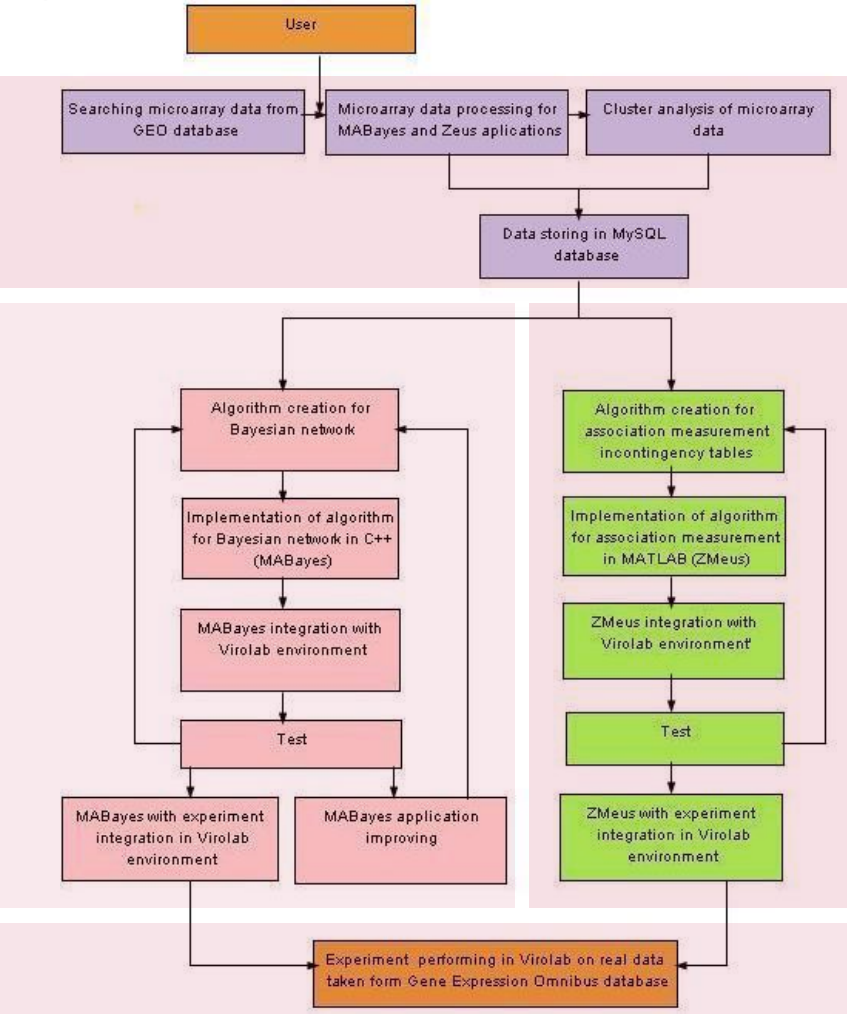
Structure of experiment

Data prossesing

Z correlation coefficient measurement

Bayesian Networks procedure

Results interpretation



Gene-biological issue association by Z-association coefficient measurement

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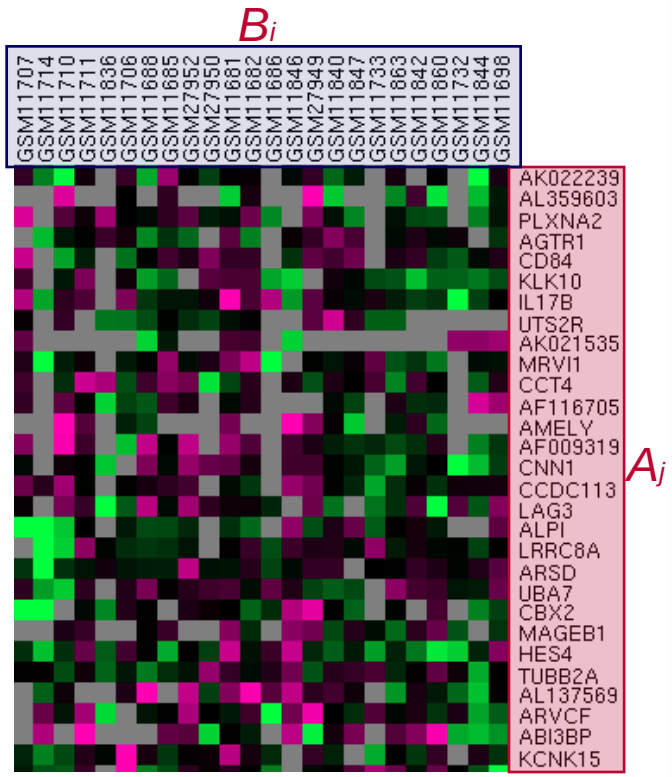
Assotiation: genes-biological issue

The method is based on a definition of dependence between two families of events: A_j and B_i

A_j : genes or group of genes (clusters)

B_i : biological issue
eg. Process, Component, Fucntion



Assotiation: genes-biological issue

The coefficient is defined on the basis of the probabilities of dependent events. It gives information about dependence between particular genes and eg. biological issue.

$$Z^2(A:B) := 1 - [P(B)\frac{1-P(A|B)}{P(\overline{A})} \cdot \frac{1-P(\overline{A}|B)}{P(A)} + P(\overline{B})\frac{1-P(A|\overline{B})}{P(\overline{A})} \cdot \frac{1-P(\overline{A}|\overline{B})}{P(A)}]$$

B→ / A↓	B_1	B_2	…	B_c	Total
A_1					$p_{1\cdot}$
A_2					$p_{2\cdot}$
⋮					⋮
A_r					$p_{r\cdot}$
Total	$p_{\cdot 1}$	$p_{\cdot 2}$	…	$p_{\cdot c}$	1

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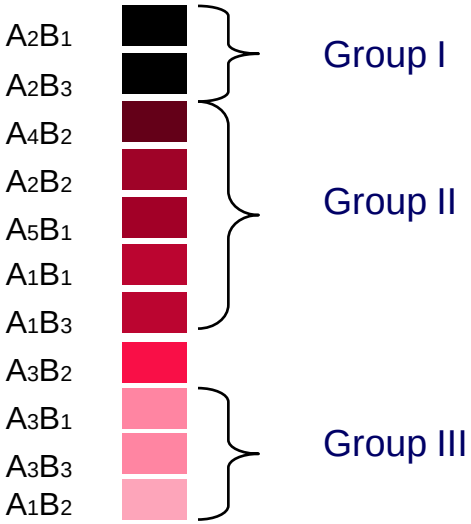
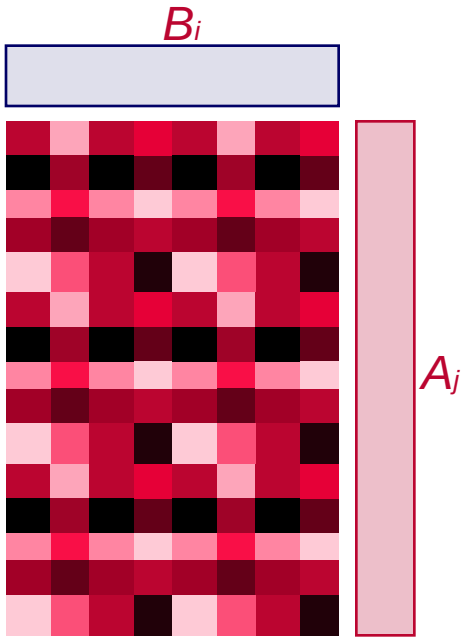


Assotiation: genes-biological issue

1. $Z(A : B_1;B_2; : : : ;B_n)$
2. $Z(A_1;A_2; : : : ;A_k : B)$
3. $Z(A_1;A_2; : : : ;A_k : B_1;B_2; : : : ;B_n)$



Bayesian Networks procedure for creation of genes-biological issue depedence networks

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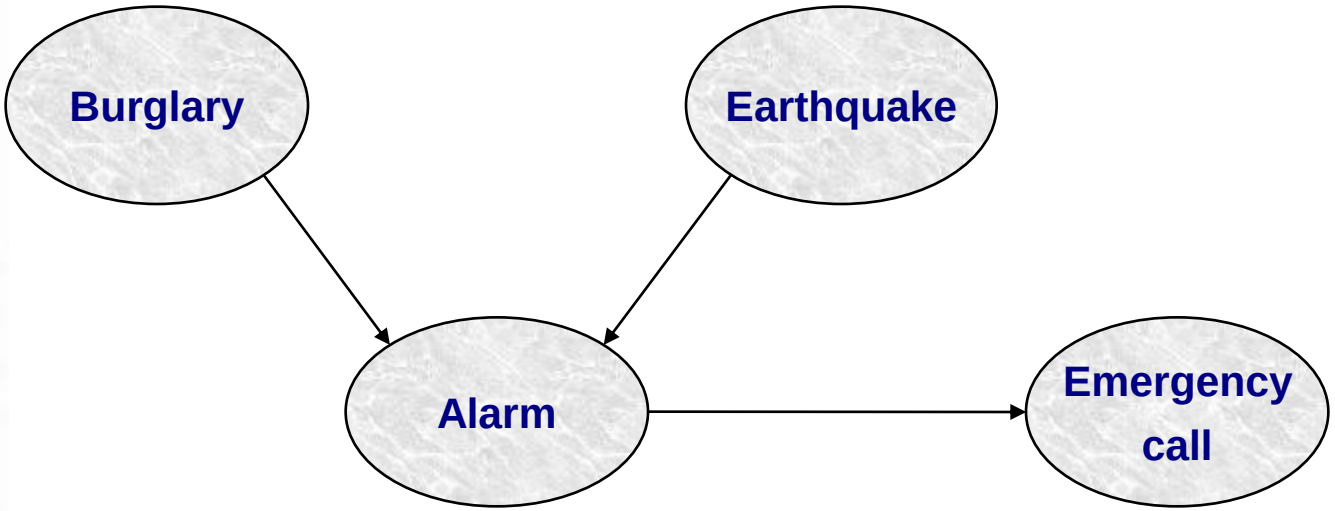
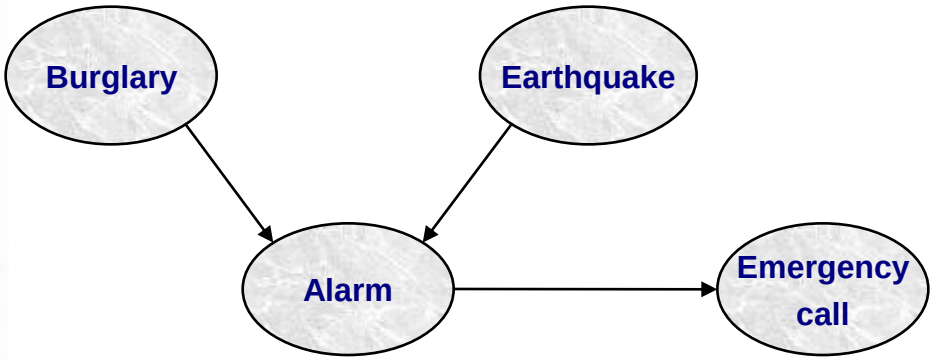
Bayesian networks provide us with a clear and simple tool for casual interactions representation



To fully describe Bayesian Network we need to know conditional distributions parameters



Probability of a burglary?

Probability of an earthquake?

Probability of running the alarm if no disaster happens?

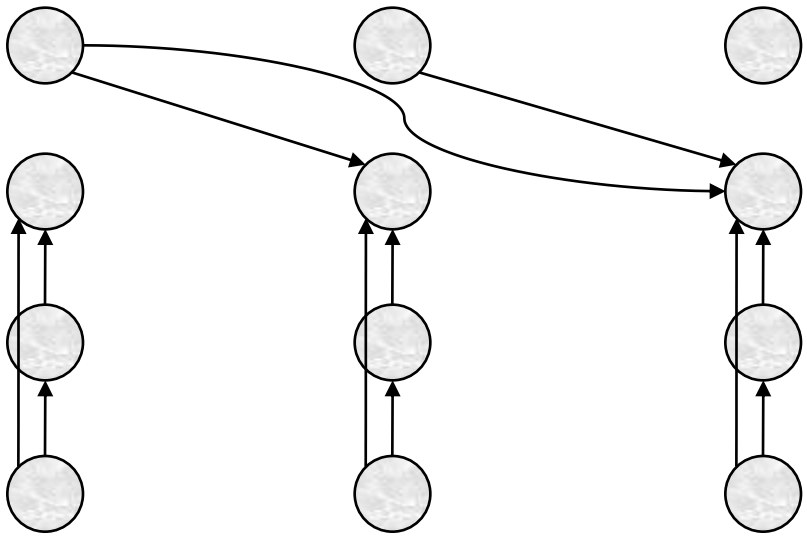
Probability of running the alarm if there was only a burglary?

etc.

Issue: Is it a correct casual interaction graph?

The major problem is to find the proper graph that would describe the phenomenon under study

Dynamic Bayesian Networks



Data from microarray experiments may be time dependent

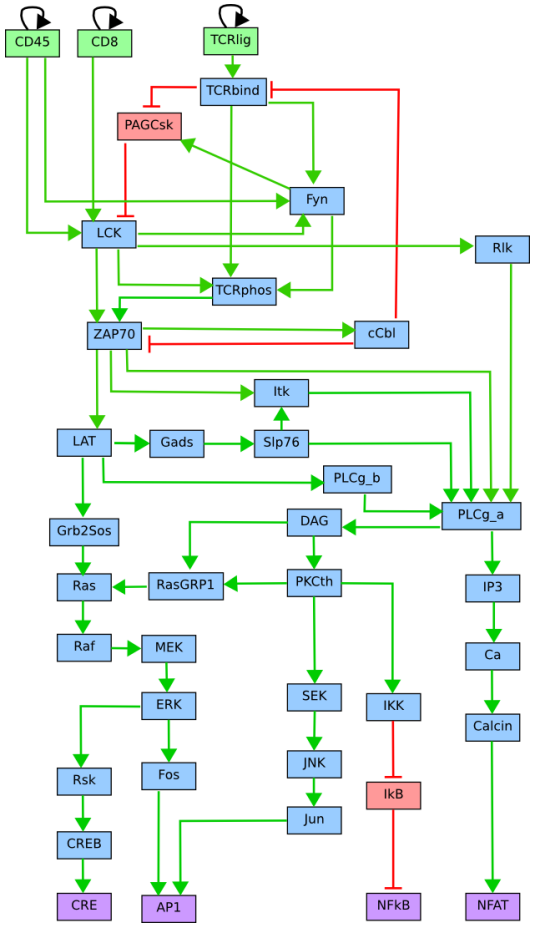
Ex. gene expression after 12, 24, 72 hours from the drug application

Bayesian Networks

Given the data (obtained from NCBI) we are interested in finding the casual interactions network

The number of possible models grows at super-exponential rate (2^{n*n}) when rising the number of nodes in the graph.

For microarray experiments the number of entities we deal with (genes, gene clusters, time step, disease stage, etc.) can reach thousands.



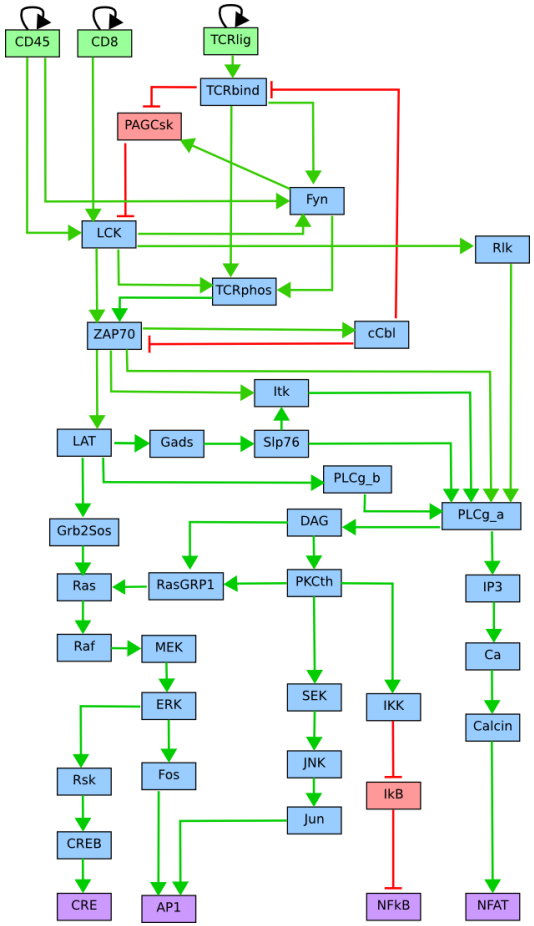
Bayesian Networks

Possible solutions for the graphical model selection problem:

- use heuristic methods which divide the problem into smaller ones
- **use Markov Chain Monte Carlo simulation to draw samples from the posterior distribution**

Calculation of the score function for the particular graph involves using complicated functions (such as the logarithm Γ-Euler function)

This together with overall complexity of the problem makes our task very computationaly demanding

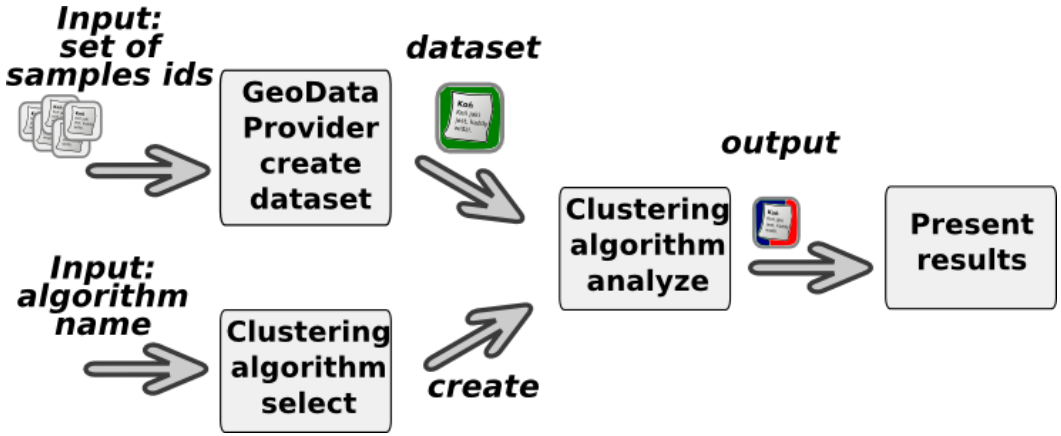


Virolab – enviroment for microarrays analysis

- Environment for development and execution of collaborative applications
- Scripting-based experiment plans (Ruby) for representing complex applications
- *Experiment Planning Environment* for experiment developers
- *Experiment Management Interface* (portal) for experiment users
- Experiment Repository, Result Management
- Access to wide range of middleware (*Grid, Web*)

- http://virolab.cyfronet.pl

- Structure of the tasks



- Available gems:
  - DataProvider – retrieves data from NCBI, allows creating new datasets
  - ClusteringAlgorithm – multiple algorithms are available (Agglomerative, Isodata, Shared Nearest Neighbor, Self-Organizing Maps, K-Means, Cobweb)
  - ClusteringAlgorithmInstrumentation – Each algorithm may be tuned by setting different cluster metrics, sample metrics, cluster representation and cluster score functions

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